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Net Flux of Glucose, Lactate, Volatile Fatty Acids, and Nitrogen Metabolites Across the Portal-Drained Viscera and Liver of Pregnant Ewes[1]

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ABSTRACT: Our objective for this study was to determine the pattern of nutrient flux across the portal-drained viscera (PDV) and liver in ewes with varying numbers of fetuses. Catheters were placed in the hepatic portal vein, a branch of the hepatic vein, a mesenteric vein, and the abdominal aorta of ewes. Blood flow and net nutrient release across the PDV and liver were determined before exposure to rams. Ewes were then mated, which resulted in two ewes not pregnant and in six ewes with single and 11 ewes with twin lambs. Additional measurements were taken 103, 82, 61, 39, 19, and 6 d before parturition. Net PDV glucose release did not differ from zero (–.4 ± 8.4 mmol/h; P = .58). In ewes with singles, premating net hepatic glucose release was 34.4 ± 2.4 mmol/h, and 19 d before parturition it was 46.2 ± 3.8 mmol/h. In ewes with twins, premating net hepatic glucose release was 36.8 ± 2.7 mmol/h, and 19 d before parturition it was 47.4 ± 2.8 mmol/h. Net PDV lactate release did not differ with litter size (P = .58) or days from parturition (P = .14; 9.7 ± 4.6 mmol/h). Net lactate uptake by the liver increased in pregnant ewes as the pregnancy progressed (P < .001). The hepatic extraction ratio for lactate increased in late pregnancy (P = .02). Net PDV and hepatic release of acetate and propionate were not different with litter size or days from parturition. Hepatic extraction ratios of VFA did not differ with litter size or day from parturition. The patterns of change in hepatic metabolite fluxes are similar to the patterns of change in gravid uterus metabolite uptake. Hepatic lactate uptake seems to be regulated during pregnancy.

Key Words: Ruminants, Sheep, Metabolism, Blood Flow

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Introduction

Nutrient demands of ewes increase exponentially during pregnancy, and the majority of the increase occurs during late pregnancy. As nutrient demand increases, weight (Fell et al., 1972) and oxygen consumption (Freetly and Ferrell, 1997) of the portal-drained viscera (**PDV**) and liver change. During pregnancy, the gravid sheep uterus is a net user of acetate, glucose, and amino acids and a net producer of ammonia, urea, and lactate (Char and Creasy, 1976; Battaglia and Meschia, 1981). The maternal liver has a central role in the regulation of all these metabolites. A knowledge of the mechanism by which ewes meet the nutrient demands of the gravid uterus is required to devise efficient strategies to feed pregnant ewes. Our objective for this study was to determine the pattern of nutrient flux across the PDV and liver in ewes with varying numbers of fetuses.

Materials and Methods

Animal Management

Details of animal management and sampling protocols have been previously presented (Freetly and Ferrell, 1997). Briefly, 19 multiparous polled Dorset ewes were individually penned. Sheep were provided water and a pelleted diet (57% dehydrated alfalfa, 28% corn cobs, and 15% corn as fed) for ad libitum consumption. A digestion study in lambs determined that the diet had an apparent digestible energy concentration of 2.09 Mcal/kg and a CP of 12% as fed (Freetly and Ferrell, 1997). Catheters were surgically placed in the portal vein, a branch of the hepatic vein, a mesenteric vein, and the abdominal aorta. Ewes were bred 54-d after surgery. Experimental procedures were conducted in accordance with the Meat Animal Research Center Animal Care Guidelines and

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the *Guide for the Care and Use of Agricultural Animals in Agricultural Research and Teaching* (Consortium 1988).

Sampling Protocol

Ewes were transferred to metabolism crates 47 d after surgery. A priming dose (15 mL) of *p*-aminohippuric acid (.15 *M*; **PAH**) was given via the mesenteric vein, followed by a constant infusion (.8 mL/min) of PAH. Sixty minutes following the priming dose, blood samples were drawn into syringes, which contained heparin (10 mL) or EDTA (5 mL), from the aortic, portal venous, and hepatic venous catheters. Samples were collected at 30-min intervals for a total of seven sets of samples per period (aortic, portal venous, and hepatic venous). Additional samples were collected as above, at 103, 82, 61, 39, 19, and 6 d before parturition.

Fresh blood samples for α-amino nitrogen, ammonia nitrogen, and urea nitrogen analysis were diluted 1:4 (vol:vol) with deionized water. Blood samples were then analyzed by automated procedures (Technicon Industrial Systems, Tarrytown NY) as described by Eisemann and Nienaber (1990). L-Lactate concentrations were determined on fresh blood using a membrane-immobilized system involving lactate oxidase (EC 1.1.3.2; Model 27, Yellow Springs Instrument Co., Yellow Springs, OH). Plasma samples for PAH and glucose analysis were diluted 1:4 (vol:vol) with deionized water. Plasma samples were analyzed for PAH and glucose by automated procedures (Technicon, 1972 No. 216-72T and No. 339-19).

Plasma flow was calculated using an indicator-dilution technique previously described (Katz and Bergman, 1969). Blood flows have previously been reported (Freetly and Ferrell, 1997). Net release of metabolites was calculated by multiplying blood or plasma flow by the concentration difference in the vessels (Katz and Bergman, 1969). A negative release rate represents a net uptake by the tissue.

Whole blood was frozen for VFA analysis. Samples within sample period and vessel were composited for each animal. Samples were prepared for gas chromatography (**GC**) analysis by deproteinization and ion exchange chromatograpy. One-hundred microliters of 7.5 m*M* 2-ethylbutyric acid was added to 4 mL of blood as an internal standard. Blood was deproteinized by adding 6 mL of (.15 *M*) BaOH and 6 mL of (.175 *M*) $ZnSO_4$ and centrifuging at 20,000 $\times$ *g* for 20 min. The supernatant was then passed over a cation exchange column that was attached to an anion exchange column. The exchange columns consisted of 8- $\times$ 40-mm polypropylene columns loaded with 100 to 200 mesh resin (Bio-Rad Laboratories, Richmond, CA). Cation columns contained 1.8 mL of AG 50W-X8 resin, and anion columns contained .6 mL of BIO-REX 5 resin (Bio-Rad). After addition of the supernatant, columns were rinsed with 10 mL of distilled water. The anion columns were then rinsed with an additional 2 mL of distilled water. Volatile fatty acids were eluted from the anion column by the addition of 12 mL of 25 m*M* NaOH. The effluent was collected and frozen. The effluent was then freeze-dried and reconstituted in .75 mL of .5 *N* hydrochloric acid.

Volatile fatty acid concentrations were determined by injecting .5 μL of the reconstituted sample on a Hewlett-Packard 5890 GC (Hewlett-Packard, Wilmington, DE). The GC was equipped with a 4-mm deactivated glass wool-packed injection sleeve and a 30 m $\times$ .25 mm Stabilwax-DA column (Restek, Bellefonte, PA). The injection port was maintained at 250°C and set for a 50:1 split with N_2. The carrier gas was H_2 and was maintained at 844 g/cm^2. Column temperature was maintained at 145°C for 5.5 min. The column was purged at the end of each run by increasing column temperature 10°C/min up to 206°C. The flame ionization detector was maintained at 250°C. The intraassay CV were 3.9, 4.5, 10.6, 6.2, 8.4, and 10.3 for acetate, propionate, 2-methyl-propionate, butyrate, 2-methyl- + 3-methyl-butyrate, and valerate, respectively. The interassay CV were 2.3, 4.1, 11.3, 3.8, 6.2, 5.7, and 9.3 for acetate, propionate, 2-methyl-propionate, butyrate, 2-methyl- + 3-methyl-butyrate, and valerate, respectively. Net fluxes of VFA were calculated by multiplying the average blood flow of the replicate samples by the concentration difference in the vessels of the composited samples.

Data were analyzed as a split plot in time with SAS GLM (1989) procedures. The model included ewe, litter size, and period as fixed effects. The model was litter size, ewe nested within litter size, period, and litter size $\times$ period. Litter size was tested with ewe nested within litter size as the source of error. Differences between least-squares means were tested with a protected *t*-test. Means and standard errors are presented in the text, tables, and figures. For the sake of discussion, responses with probabilities less than .05 are considered to be different.

Results

Two ewes did not give birth to lambs (**Nonpregnant**). Six ewes gave birth to single (**Single**) lambs, and 11 ewes gave birth to twins (**Twin**). Over the course of the study, some of the ewes had catheters that failed to work. One ewe in the Single group had a catheter in the hepatic vein that failed to function during Periods 5 and 7. In the Twin group, one ewe was removed from study after Period 3, and a second ewe was removed after Period 4 owing to failure of the abdominal aortal catheter. One ewe in the Twin group lambed before Period 7 and, therefore, was not

sampled during Period 7. Some of the catheters became difficult to sample during the course of the study, which resulted in a limited amount of blood at a given time point. In the cases in which blood was limiting, not all chemistries were conducted for a given sample. Urea N and ammonia N were not analyzed in Period 1. Feed intake tended to decrease during pregnancy and BW increased (Freetly and Ferrell, 1997). Plasma flow (Table 1) followed the same pattern as blood flow (Freetly and Ferrell, 1997).

Glucose

Arterial (3.48 ± .05 m*M*), portal venous (3.48 ± .05 m*M*), and hepatic venous (3.75 ± .05 m*M*) glucose concentrations did not differ with days from parturition or litter size (Table 2). Net PDV glucose release (−.4 ± .7 mmol/h; Table 2) did not differ with litter size or days from parturition, nor did it differ from zero ($P = .58$). Net hepatic glucose release (37.6 ± 1.0 mmol/h) tended to be greater in pregnant ewes ($P = .08$; Figure 1). Splanchnic glucose release tended to increase in latter periods ($P = .06$; Table 2).

Lactate

Blood lactate concentrations were higher 39 d before parturition; arterial and portal lactate concentrations before parturition were higher at 6, 19, and 39 d than they were at 151 d (Table 3). There was a net release of lactate from the PDV (9.7 ± .4 mmol/h; $P < .001$), but it did not differ with days from parturition or litter size (Table 4). Net lactate uptake by the liver increased in pregnant ewes as the pregnancy progressed (Figure 2). There was a net release of lactate from splanchnic tissues in the nonpregnant ewes and in pregnant ewes in early pregnancy; however, in late pregnancy, there was a net uptake of lactate by the splanchnic tissues (Table 4). Hepatic extraction ratios did not differ ($P > .70$) with litter size before ewes were mated (151 d; .06 ± .01), but, by late pregnancy, ewes with singles (6 d; .26 ± .05) and twins (6 d; .23 ± .03) had higher extraction ratios ($P < .001$) than did nonpregnant ewes (6 d; .01 ± .03).

Ammonia

Arterial and hepatic venous ammonia concentrations were higher at 6 and 19 d before parturition than in other periods (Table 3). Portal venous ammonia concentration was lowest 151 d from parturition ($P < .001$), but other periods did not differ from each other. Both net ammonia PDV release and hepatic uptake 151 d from parturition were lower than they were 19 through 103 d from parturition and did not differ from 6 d from parturition (Table 4). There was a net uptake of ammonia across the splanchnic tissues (.80 ± .05 mmol/h; $P < .001$), but it did not differ with days from parturition or litter size (Table 4). Ewes that did not have lambs had a higher hepatic ammonia extraction ratio (.69 ± .02) than ewes with single (.62 ± .02) or twin (.61 ± .02) lambs ($P = .02$). Hepatic extraction ratio differed with days from parturition ($P < .001$) and followed a pattern similar to net hepatic ammonia uptake.

α-*Amino Nitrogen*

Arterial, portal venous, and hepatic venous α-amino nitrogen concentration were highest 19 d from parturi-

Table 1. Means and standard errors for plasma flow (L-h) across the portal-drained viscera and liver of pregnant ewes

Plasma flow and litter size[a]	Period and days before parturition: 1 151 ± 1	2 103 ± 1	3 82 ± 1	4 61 ± 1	5 39 ± 1	6 19 ± 1	7 6 ± 1	Probability: Litter	Period	L × P
	L/h									
Hepatic arterial								.89	.28	.96
0	8.9 ± 10.8	20.5 ± 10.7	17.6 ± 2.2	10.2 ± 2.4	23.3 ± 2.3	27.0 ± 1.9	26.8 ± 2.1			
1	9.7 ± 2.2	16.5 ± 6.7	20.3 ± 3.1	21.3 ± 4.2	23.4 ± 7.0	25.5 ± 5.7	19.2 ± 6.8			
2	17.8 ± 2.7	26.0 ± 6.0	21.7 ± 4.2	22.9 ± 3.2	18.0 ± 3.1	24.7 ± 4.8	29.4 ± 4.3			
Portal venous								.04	.006	.36
0	130.2 ± 20.8	125.2 ± 8.2	95.6 ± 13.5	103.6 ± 18.8	76.0 ± 4.6	108.6 ± 3.0	106.6 ± 12.3			
1	133.9 ± 6.1	125.4 ± 9.3	113.2 ± 4.6	118.4 ± 7.4	121.1 ± 11.9	135.8 ± 9.7	121.0 ± 10.8			
2	132.9 ± 7.0	127.4 ± 9.4	107.1 ± 7.3	111.1 ± 7.2	124.8 ± 7.7	133.8 ± 10.9	138.2 ± 8.3			
Hepatic venous								.16	.007	.50
0	139.1 ± 10.0	145.6 ± 18.9	113.2 ± 11.3	113.8 ± 16.4	99.2 ± 6.8	135.5 ± 4.8	133.3 ± 14.3			
1	143.6 ± 6.0	141.9 ± 3.9	133.5 ± 4.0	139.7 ± 6.0	136.5 ± 8.9	152.4 ± 4.2	130.3 ± 11.5			
2	150.6 ± 7.4	153.4 ± 10.2	128.8 ± 7.7	134.0 ± 6.0	142.9 ± 6.6	158.5 ± 11.7	167.6 ± 8.8			

[a]Litter size 0 (n = 2). Litter size 1: Periods 1 through 4 (n = 6), Periods 5 and 7 arterial and hepatic venous (n = 5) and portal venous (n = 6); and Period 6 arterial and hepatic venous (n = 4) portal venous (n = 5). Litter size 2: Periods 1 and 3 (n = 11), Periods 2 and 4 (n = 10), Periods 5 and 6 (n = 9), and Period 7 (n = 8).

tion (Table 3). There was a net release of α-amino nitrogen across the PDV (36.7 ± 1.8 mmol/h; $P < .001$) and a net uptake of α-amino nitrogen liver across the liver (37.1 ± 1.6 mmol/h; $P < .001$), but neither differed with litter size or days from parturition (Table 4). Net release of α-amino nitrogen across the splanchnic tissues (−.6 ± 1.3 mmol/h; $P = .66$) did not differ from zero. The hepatic extraction ratio for α-amino nitrogen did not differ with number of lambs (.05 ± .01) but was lower at 6 d (.03 ± .003) and 19 d (.03 ± .003) before parturition than in periods closer to mating (period; $P < .001$).

Urea

Arterial, portal venous, and hepatic venous urea nitrogen concentration were lower 6 and 19 d before parturition than in other periods (Table 3). There was a net uptake of urea N across the PDV (9.2 ± 1.0 mmol/h; $P < .001$), but it did not differ with litter size or days from parturition (Table 4). Net hepatic and splanchnic urea N release were at their highest 103 d before parturition and at their lowest 6 d before parturition (Table 4).

Acetate

Arterial (1.082 ± .03 m*M*) and portal venous (2.050 ± .04 m*M*) acetate concentration did not differ with litter size or days from parturition (Table 5); however, hepatic venous concentrations were lower at 6 d before parturition than in periods further than 39 d before parturiton (Table 5). There was a net release of acetate by the PDV (156.3 ± 4.9 mmol/h; $P < .001$), liver (5.5 ± 2.2 mmol/h; $P = .02$), and splanchnic tissues (158.5 ± 4.6 mmol/h; $P < .001$), but they did not differ with litter size or day from parturition (Table 6).

Propionate

Propionate concentrations did not differ in the artery (.034 ± .001 m*M*), portal vein (.295 ± .008 m*M*), and hepatic vein (.050 ± .002 m*M*) with litter size or days from parturition (Table 5). There was a

Table 2. Means and standard errors for plasma glucose concentration (m*M*) and net release across the portal-drained viscera (PDV) and liver (mmol/h) of pregnant ewes

Item and litter size[a]	Period and days before parturition: 1 151 ± 1	2 103 ± 1	3 82 ± 1	4 61 ± 1	5 39 ± 1	6 19 ± 1	7 6 ± 1	Probability: Litter	Period	L × P
	Concentration, m*M*									
Arterial								.32	.12	.36
0	3.46 ± .12	3.51 ± .05	3.44 ± .01	3.39 ± .10	3.37 ± .03	3.63 ± .02	3.52 ± .09			
1	3.74 ± .11	3.78 ± .18	3.60 ± .21	3.54 ± .17	3.78 ± .33	3.58 ± .14	3.28 ± .30			
2	3.75 ± .08	3.67 ± .09	3.51 ± .11	3.53 ± .09	3.31 ± .13	3.06 ± .20	2.71 ± .30			
Portal venous								.32	.09	.33
0	3.46 ± .12	3.54 ± .09	3.39 ± .04	3.37 ± .09	3.25 ± .04	3.65 ± .03	3.48 ± .04			
1	3.72 ± .11	3.77 ± .17	3.60 ± .22	3.55 ± .17	3.75 ± .34	3.60 ± .16	3.27 ± .31			
2	3.76 ± .08	3.64 ± .08	3.55 ± .08	3.56 ± .09	3.32 ± .14	3.11 ± .21	2.68 ± .29			
Hepatic venous								.32	.17	.39
0	3.68 ± .19	3.71 ± .05	3.64 ± .04	3.59 ± .10	3.50 ± .05	3.88 ± .04	3.70 ± .10			
1	3.97 ± .09	4.00 ± .16	3.95 ± .22	3.80 ± .18	4.14 ± .40	3.92 ± .19	3.50 ± .38			
2	4.01 ± .08	3.87 ± .09	3.81 ± .09	3.85 ± .09	3.64 ± .14	3.41 ± .19	2.98 ± .32			
	Release, mmol/h									
PDV								.93	.58	.85
0	−1.1 ± 1.8	4.1 ± 5.7	−4.3 ± 2.4	−1.9 ± 2.0	−9.2 ± 1.8	1.2 ± .5	−3.1 ± 6.6			
1	−3.1 ± 1.9	−.6 ± 2.9	−1.0 ± 1.5	.7 ± 2.7	−4.2 ± 3.4	.3 ± 4.6	−1.6 ± 3.2			
2	.5 ± 2.2	−3.7 ± 2.2	2.1 ± 4.0	2.8 ± 3.2	.5 ± 1.8	5.5 ± 3.3	−4.7 ± 3.1			
Hepatic								.07	.12	.63
0	32.7 ± 10.4	25.5 ± 1.9	27.0 ± 3.1	24.2 ± 4.2	22.2 ± 1.9	31.4 ± 2.4	25.2 ± 7.5			
1	34.4 ± 2.4	32.0 ± 3.7	36.2 ± 3.0	35.3 ± 3.2	41.3 ± 2.8	46.2 ± 3.8	36.2 ± 6.3			
2	36.8 ± 2.7	34.3 ± 2.7	34.6 ± 2.5	38.9 ± 2.4	45.2 ± 1.5	47.4 ± 2.8	48.2 ± 5.9			
Splanchnic								.11	.06	.56
0	31.6 ± 12.2	29.6 ± 3.9	22.7 ± 5.4	22.3 ± 2.2	13.0 ± 3.7	32.4 ± 2.8	22.1 ± .9			
1	31.2 ± 3.2	31.5 ± 6.1	35.2 ± 4.1	36.0 ± 3.2	37.7 ± 3.0	50.1 ± 2.4	33.6 ± 4.8			
2	37.3 ± 3.2	30.7 ± 4.2	36.7 ± 3.8	41.6 ± 3.7	45.7 ± 2.0	52.8 ± 4.7	43.5 ± 5.1			

[a]Litter size 0 (n = 2). Litter size 1: Periods 1 through 4 (n = 6); Periods 5 and 7 hepatic venous, hepatic release, and splanchnic release (n = 5) and arterial, portal venous, and portal drained-viscera release (n = 6); and Period 6 hepatic venous, hepatic release, and splanchnic release (n = 4) arterial, portal venous and portal-drained viscera (n = 5). Litter size 2: Periods 1 and 3 (n = 11), Periods 2 and 4 (n = 10), Periods 5 and 6 (n = 9), and Period 7 (n = 8).

net release of propionate across the PDV (42.2 ± 1.5 mmol/h; $P < .001$) and splanchnic tissues (3.0 ± .2 mmol/h; $P < .001$), but they did not differ with litter size or days from parturition (Table 6). There was a net propionate uptake across the liver (38.5 ± 1.5 mmol/h; $P < .001$), but it did not differ with litter size or days from parturition (Table 6). The propionate hepatic extraction ratio (.78 ± .02) did not differ with litter size ($P = .22$) or with days from parturition ($P = .53$).

2-Methyl-propionate

2-Methyl-propionate concentrations did not differ in the artery (.003 ± .001 m*M*) and hepatic vein (.004 ± .0002 m*M*) between litter size or with days from parturition, but portal vein 2-methyl-propionate concentrations were lower 6 and 19 d before parturition than in periods earlier than 39 d before parturition (Table 5). Net release of 2-methyl-propionate across the PDV and net uptake across the liver did not differ with litter size but were lower 6 d before parturition than at other periods (Table 6). There was a net splanchnic tissue release (.07 ± .03 mmol/h; $P = .02$). The 2-methyl-propionate hepatic extraction ratio (.71 ± .02) did not differ with litter size ($P = .97$) or days from parturition ($P = .56$).

Butyrate

Arterial, portal venous, and hepatic venous butyrate concentrations were lower 6 and 19 d before parturition than those early in the study (Table 5). Net PDV butyrate release before mating (9.8 ± 1.2 mmol/h) was higher than in other periods (Table 6). Net hepatic butyrate uptake 6 d before parturition was lower than net hepatic uptakes 151 through 61 d before parturition (Table 6). The butyrate hepatic extraction rate ratio (.51 ± .02) did not differ with litter size ($P = .38$) or days from parturition ($P = .27$). Net splanchnic butyrate release was greater 151 d before parturition than in subsequent periods (Table 6).

2-Methyl- and 3-Methyl-butyrate

Combined 2-methyl- and 3-methyl-butyrate arterial (.006 ± .0002 m*M*) and hepatic venous (.008 ± .0005 m*M*) concentrations did not differ with litter size or days from parturition (Table 5), but portal venous concentrations decreased in late pregnancy (Table 5). Net PDV release of 2-methyl- and 3-methyl-butyrate was lower at 6 d before parturition (1.1 ± .1 mmol/h) than at 103 (2.3 ± .3 mmol/h) and 151 d (2.6 ± .4 mmol/h) before parturition (Table 6). There was a net hepatic uptake (1.6 ± .1 mmol/h; $P < .001$), but it did not differ with litter size or days from parturition (Table 6). The hepatic extraction ratio (.52 ± .02) did not differ with litter size ($P = .86$) or days from parturition ($P = .49$). There was a net splanchnic release (.3 ± .1 mmol/h; $P = .002$), but it did not differ with litter size or days from parturition (Table 6).

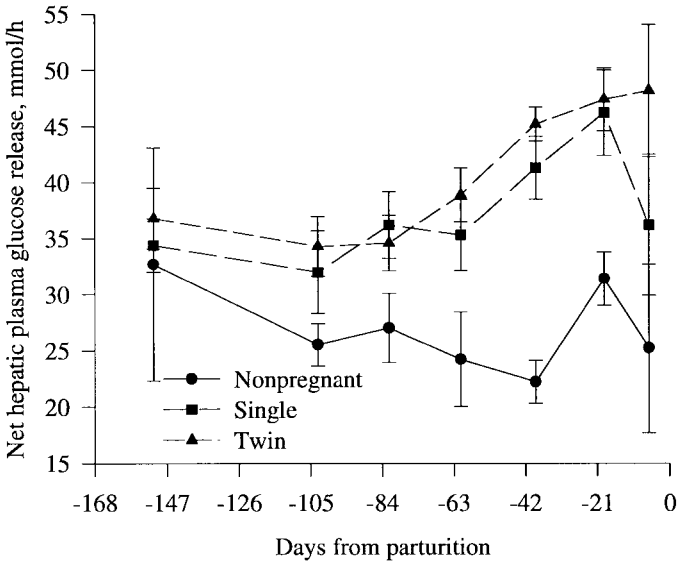

Figure 1. Means and standard errors for net hepatic glucose release of ewes. Nonpregnant (n = 2). Single: –151 to –61 d (n = 6), –39 d and –6 d (n = 5), and –19 d (n = 4). Twins: –151 and –82 d (n = 11), –103 and –61 d (n = 10), –39 and –19 d (n = 9), and –6 d (n = 8).

Valerate

Arterial (.002 ± .0001 m*M*) and hepatic venous (.002 ± .0001 m*M*) valerate concentrations did not differ with litter size or days from parturition. Portal venous valerate concentration 6 d before parturition (.006 ± .001 m*M*) was lower than at 151 d (.01 ± .001 m*M*). Net release of valerate across the PDV and net uptake by the liver was greater 151 d before parturition than closer to parturition. There was a net splanchnic valerate uptake (.08 ± .02 mmol/h; $P < .001$), but it did not differ with litter size or days from parturition (Table 6). The valerate hepatic extraction ratio (.76 ± .02) did not differ with litter size ($P = .64$) or days from parturition ($P = .11$).

Discussion

Slaughter and calorimetric trials have been used to estimate the energy and protein requirement of ewes during pregnancy (Graham, 1964; Langlands and Sutherland, 1968; Rattray et al., 1974). Nutrient flux studies have quantified specific nutrient requirements of the gravid uterus at various stages of pregnancy (Battaglia and Meschia, 1981; Bell et al., 1986). The nutrient demands of the gravid uterus suggest that the number of fetuses and stage of pregnancy will

Table 3. Means and standard errors for blood concentration (m*M*) of lactate and nitrogen metabolites in pregnant ewes

Item and litter size[a]	Period and days before parturition: 1 151 ± 1	2 103 ± 1	3 82 ± 1	4 61 ± 1	5 39 ± 1	6 19 ± 1	7 6 ± 1	Probability: Litter	Period	L × P
Lactate										
Arterial								.22	.003	.94
0	.46 ± .01	.53 ± .02	.44 ± .02	.49 ± .02	.60 ± .06	.58 ± .02	.58 ± .11			
1	.47 ± .03	.59 ± .07	.61 ± .11	.58 ± .05	.97 ± .25	.65 ± .04	.65 ± .07			
2	.42 ± .02	.49 ± .03	.49 ± .03	.61 ± .05	.83 ± .08	.66 ± .04	.62 ± .08			
Portal venous								.18	.009	.94
0	.50 ± .01	.58 ± .03	.51 ± .02	.55 ± .03	.68 ± .09	.64 ± .01	.65 ± .13			
1	.52 ± .03	.64 ± .07	.67 ± .11	.64 ± .05	1.00 ± .22	.70 ± .04	.72 ± .07			
2	.48 ± .02	.55 ± .03	.55 ± .03	.69 ± .05	.88 ± .08	.75 ± .04	.69 ± .08			
Hepatic venous								.23	.006	.91
0	.51 ± .01	.61 ± .04	.52 ± .00	.56 ± .05	.68 ± .09	.63 ± .02	.64 ± .15			
1	.55 ± .03	.67 ± .07	.66 ± .09	.62 ± .03	1.02 ± .27	.63 ± .04	.57 ± .08			
2	.50 ± .03	.58 ± .03	.54 ± .03	.66 ± .04	.82 ± .08	.60 ± .06	.53 ± .07			
Ammonia N										
Arterial								.51	.0001	.99
0	.05 ± .002	.05 ± .003	.05 ± .01	.04 ± .01	.05 ± .001	.07 ± .01	.08 ± .01			
1	.06 ± .01	.05 ± .01	.06 ± .002	.06 ± .01	.06 ± .004	.09 ± .01	.10 ± .004			
2	.06 ± .004	.05 ± .003	.06 ± .003	.05 ± .003	.05 ± .003	.08 ± .004	.09 ± .005			
Portal venous								.89	.0001	.96
0	.13 ± .01	.19 ± .01	.19 ± .01	.18 ± .02	.18 ± .001	.20 ± .01	.19 ± .01			
1	.13 ± .01	.18 ± .01	.19 ± .01	.18 ± .01	.19 ± .01	.18 ± .02	.17 ± .01			
2	.13 ± .01	.18 ± .01	.18 ± .01	.18 ± .004	.17 ± .01	.16 ± .01	.18 ± .01			
Hepatic venous								.37	.0001	.97
0	.05 ± .002	.04 ± .004	.05 ± .01	.04 ± .01	.04 ± .00	.06 ± .01	.07 ± .01			
1	.06 ± .01	.05 ± .01	.05 ± .003	.05 ± .01	.05 ± .005	.08 ± .01	.10 ± .005			
2	.06 ± .003	.04 ± .002	.05 ± .003	.04 ± .003	.05 ± .003	.07 ± .004	.09 ± .01			
α-Amino N										
Arterial								.24	.0001	1.00
0		3.86 ± .03	3.91 ± .13	3.84 ± .33	3.90 ± .15	4.79 ± .13	3.71 ± .11			
1		3.98 ± .18	4.03 ± .13	4.24 ± .20	3.81 ± .12	5.00 ± .26	4.09 ± .17			
2		4.05 ± .10	4.03 ± .14	4.21 ± .16	4.13 ± .19	4.92 ± .18	4.12 ± .17			
Portal venous								.29	.0001	1.00
0		4.06 ± .05	4.12 ± .18	4.08 ± .38	3.66 ± .05	5.06 ± .19	3.81 ± .16			
1		4.24 ± .21	4.30 ± .15	4.50 ± .21	4.11 ± .19	5.25 ± .32	4.27 ± .21			
2		4.31 ± .11	4.28 ± .14	4.47 ± .18	4.35 ± .20	5.15 ± .20	4.28 ± .20			
Hepatic venous								.27	.0001	.99
0		3.86 ± .02	3.87 ± .14	3.81 ± .34	3.43 ± .00	4.74 ± .12	3.60 ± .13			
1		3.96 ± .19	4.11 ± .12	4.20 ± .21	3.88 ± .20	4.99 ± .28	3.08 ± .18			
2		4.04 ± .09	4.04 ± .13	4.18 ± .17	4.11 ± .19	5.01 ± .18	4.15 ± .20			
Urea N										
Arterial								.15	.0001	.32
0		5.48 ± .01	5.23 ± .34	5.39 ± .10	4.94 ± .12	5.01 ± .27	5.24 ± .23			
1		5.79 ± .10	5.72 ± .27	5.16 ± .33	5.18 ± .35	3.96 ± .45	3.83 ± .34			
2		5.53 ± .15	5.20 ± .26	5.06 ± .26	4.69 ± .24	3.55 ± .24	3.26 ± .25			
Portal venous								.18	.0001	.29
0		5.37 ± .04	5.10 ± .33	5.28 ± .13	4.86 ± .12	4.96 ± .29	5.16 ± .26			
1		5.74 ± .12	5.64 ± .26	5.09 ± .34	5.09 ± .34	3.89 ± .45	3.77 ± .34			
2		5.51 ± .15	5.16 ± .26	4.98 ± .27	4.60 ± .24	3.53 ± .24	3.21 ± .25			
Hepatic venous								.17	.0001	.29
0		5.63 ± .05	5.34 ± .33	5.53 ± .11	5.10 ± .13	5.17 ± .30	5.38 ± .23			
1		6.00 ± .12	5.80 ± .27	5.33 ± .34	5.44 ± .42	4.03 ± .47	3.98 ± .41			
2		5.75 ± .15	5.35 ± .29	5.22 ± .27	4.79 ± .24	3.65 ± .25	3.31 ± .26			

[a]Litter size 0 (n = 2), Litter size 1: Periods 1 through 4 and 6 (n = 6), Periods 5 and 7 arterial and portal venous (n = 6) and hepatic venous (n = 5). Litter size 2: Periods 1 through 3 (n = 11), Period 4 (n = 10), Periods 5 and 6 (n = 9), and Period 7 (n = 8).

Table 4. Means and standard errors for net release (mmol/h) of blood lactate and nitrogen metabolites across the portal-drained viscera and liver of pregnant ewes

Item and litter size[a]	Period and days before parturition: 1 151 ± 1	2 103 ± 1	3 82 ± 1	4 61 ± 1	5 39 ± 1	6 19 ± 1	7 6 ± 1	Probability: Litter	Period	L × P
Lactate										
Portal-drained viscera								.58	.14	.90
0	6.1 ± 1.6	9.0 ± .8	8.1 ± 1.4	9.2 ± 3.8	7.5 ± 3.3	8.5 ± 2.0	10.2 ± 1.7			
1	8.2 ± .7	7.4 ± 1.4	8.1 ± .7	9.0 ± .5	4.0 ± 5.2	10.2 ± 3.1	11.0 ± 1.2			
2	9.9 ± 1.2	9.6 ± 1.5	8.4 ± .7	11.6 ± 1.6	9.0 ± .8	15.6 ± 1.4	12.3 ± 1.6			
Hepatic								.16	.0001	.0005
0	3.3 ± 1.7	5.1 ± .5	4.1 ± 2.7	1.3 ± 1.3	2.4 ± 1.4	.7 ± 5.3	–.7 ± 3.2			
1	4.8 ± 1.3	6.8 ± 1.4	1.0 ± 3.5	–.4 ± 4.3	–8.2 ± 6.3	–12.0 ± 4.5	–28.8 ± 3.4			
2	5.8 ± 1.0	6.6 ± 1.3	.7 ± 2.0	–3.6 ± 2.8	–10.1 ± 2.4	–28.3 ± 3.4	–30.6 ± 3.3			
Splanchnic								.67	.0001	.02
0	9.4 ± 3.3	14.1 ± .4	12.2 ± 4.1	10.5 ± 5.1	9.9 ± 4.7	9.2 ± 7.3	9.6 ± 4.9			
1	13.0 ± 1.6	14.1 ± 2.3	9.1 ± 3.0	8.6 ± 4.2	–5.2 ± 7.4	–1.8 ± 6.4	–18.3 ± 3.6			
2	15.6 ± 1.4	16.2 ± 1.7	9.1 ± 1.8	8.0 ± 2.2	–1.1 ± 2.8	–12.7 ± 4.1	–18.3 ± 3.5			
Ammonia N										
Portal-drained viscera								.66	.0001	.59
0	13.0 ± 3.7	27.1 ± 4.7	16.6 ± 2.8	18.6 ± 4.6	11.9 ± 1.1	19.3 ± .7	15.6 ± .8			
1	11.9 ± .6	21.6 ± 2.5	19.2 ± 1.2	18.8 ± 1.5	20.4 ± 3.0	15.7 ± 2.6	14.7 ± 2.6			
2	11.0 ± .7	20.1 ± 1.4	18.6 ± 1.5	19.0 ± 1.2	18.4 ± 1.5	17.2 ± 2.2	12.8 ± 1.3			
Hepatic								.64	.0001	.57
0	–13.5 ± 3.8	–28.0 ± 5.0	–17.0 ± 2.5	–19.0 ± 4.2	–12.7 ± 1.1	–20.1 ± .7	–16.4 ± .8			
1	–12.6 ± .7	–22.7 ± 2.4	–20.1 ± 1.2	–19.8 ± 1.5	–20.8 ± 3.5	–16.6 ± 2.7	–13.4 ± 2.1			
2	–11.6 ± .8	–20.9 ± 1.4	–19.5 ± 1.5	–19.8 ± 1.2	–19.6 ± 1.4	–17.6 ± 2.2	–13.5 ± 1.3			
Splanchnic								.53	.28	.94
0	–.5 ± .1	–.9 ± .3	–.4 ± .3	–.5 ± .4	–.9 ± .0	–.8 ± .0	–.8 ± .0			
1	–.7 ± .1	–1.1 ± .2	–.9 ± .1	–1.1 ± .1	–1.3 ± .2	–.9 ± .2	–.5 ± .3			
2	–.6 ± .3	–.8 ± .2	–.8 ± .3	–.8 ± .1	–1.2 ± .2	–.4 ± .2	–.6 ± .2			
α-Amino N										
Portal-drained viscera								.57	.09	1.00
0		39.5 ± 8.7	26.7 ± 11.0	33.1 ± 11.2	15.1 ± 1.1	39.9 ± 5.8	14.6 ± 4.1			
1		42.6 ± 9.0	39.8 ± 4.5	39.3 ± 5.7	32.2 ± 8.7	45.0 ± 13.0	29.7 ± 10.5			
2		39.1 ± 2.6	36.1 ± 3.8	38.8 ± 4.6	35.2 ± 3.1	47.8 ± 9.7	27.9 ± 6.1			
Hepatic								.49	.10	.65
0		–38.3 ± 4.5	–32.2 ± 9.3	–38.1 ± 11.1	–24.2 ± 7.1	–50.7 ± 9.0	–32.7 ± .0			
1		–45.8 ± 7.3	–42.2 ± 4.8	–44.4 ± 5.9	–37.4 ± 7.3	–45.5 ± 11.0	–20.9 ± 3.0			
2		–41.5 ± 4.4	–36.2 ± 4.3	–43.3 ± 4.3	–38.2 ± 3.9	–28.2 ± 8.3	–22.0 ± 3.6			
Splanchnic								.93	.63	.15
0		1.2 ± 4.1	–5.4 ± 1.7	–5.0 ± .1	–9.1 ± 6.0	–10.9 ± 3.2	–18.1 ± 4.0			
1		–3.2 ± 3.8	–2.4 ± 1.8	–5.2 ± 2.7	–4.2 ± 3.7	–.5 ± 10.0	–.2 ± 4.6			
2		–2.4 ± 3.1	–.2 ± 5.0	–4.6 ± 1.8	–3.0 ± 1.6	19.6 ± 6.0	5.9 ± 5.7			
Urea N										
Portal-drained viscera								.89	.80	.82
0		–19.9 ± .3	–15.0 ± 1.5	–15.1 ± 6.4	–7.7 ± .2	–6.1 ± 4.2	–9.6 ± 2.8			
1		–7.8 ± 4.7	–11.0 ± 3.8	–10.1 ± 3.7	–15.2 ± 3.6	–11.8 ± 2.6	–10.8 ± 3.5			
2		–4.1 ± 3.9	–6.8 ± 5.4	–11.0 ± 1.8	–13.5 ± 2.1	–3.3 ± 4.1	–7.2 ± 2.2			
Hepatic								.47	.002	.65
0		51.0 ± 13.8	31.4 ± 4.8	34.1 ± 8.2	26.4 ± .2	36.0 ± 1.5	32.8 ± 1.5			
1		46.4 ± 5.2	41.2 ± 4.0	38.5 ± 3.6	42.2 ± 6.3	26.4 ± 6.9	18.6 ± 3.0			
2		43.3 ± 3.1	32.2 ± 6.6	40.0 ± 2.3	32.5 ± 3.0	26.3 ± 3.7	19.6 ± 3.9			
Splanchnic								.70	.03	.62
0		31.1 ± 14.0	16.4 ± 3.3	19.0 ± 1.8	18.7 ± .4	29.9 ± 5.7	23.1 ± 1.3			
1		38.6 ± 6.4	30.2 ± 3.9	28.4 ± 3.5	29.0 ± 2.9	14.6 ± 7.1	10.1 ± 2.2			
2		39.3 ± 3.1	25.4 ± 9.3	29.0 ± 2.6	19.1 ± 2.7	23.0 ± 5.6	12.5 ± 3.7			

[a]Litter size 0 (n = 2). Litter size 1: Periods 1 through 4 and 6 (n = 6), Period 5 and 7 portal-drained viscera (n = 6) and hepatic and splanchnic (n = 5). Litter size 2: Periods 1 through 3 (n = 11), Period 4 (n = 10), Periods 5 and 6 (n = 9), and Period 7 (n = 8).

Table 5. Means and standard errors for concentration (m*M*) of blood volatile fatty acids in pregnant ewes

Item and litter size[a]	Period and days before parturition: 1 151 ± 1	2 103 ± 1	3 82 ± 1	4 61 ± 1	5 39 ± 1	6 19 ± 1	7 6 ± 1	Probability: Litter	Period	L × P
Acetate										
Arterial								.64	.17	.91
0	1.216 ± .287	.985 ± .150	.952 ± .063	.980 ± .090	.821 ± .079	.847 ± .100	.684 ± .008			
1	1.218 ± .138	1.159 ± .128	1.151 ± .152	1.157 ± .192	1.055 ± .152	1.051 ± .171	.995 ± .146			
2	1.106 ± .078	1.013 ± .048	1.121 ± .028	1.202 ± .070	1.216 ± .077	1.120 ± .059	.938 ± .110			
Portal venous								.63	.09	.96
0	2.201 ± .539	1.837 ± .325	1.799 ± .184	1.968 ± .231	1.660 ± .155	1.669 ± .092	1.512 ± .021			
1	2.243 ± .190	2.196 ± .190	2.112 ± .218	2.223 ± .246	2.069 ± .211	2.007 ± .335	1.854 ± .322			
2	2.091 ± .114	2.008 ± .067	2.175 ± .071	2.287 ± .074	2.285 ± .097	2.069 ± .083	1.627 ± .224			
Hepatic venous								.51	.05	.51
0	2.118 ± .539	1.772 ± .250	1.740 ± .149	1.814 ± .175	1.602 ± .089	1.551 ± .138	1.344 ± .041			
1	2.067 ± .233	2.056 ± .175	1.974 ± .216	2.067 ± .252	1.913 ± .277	1.766 ± .346	1.571 ± .215			
2	2.036 ± .177	1.923 ± .056	2.102 ± .054	2.164 ± .068	2.188 ± .100	1.971 ± .076	1.625 ± .223			
Propionate										
Arterial								.80	.20	.99
0	.029 ± .007	.022 ± .004	.030 ± .007	.022 ± .006	.018 ± .0004	.027 ± .007	.017 ± .001			
1	.049 ± .013	.039 ± .004	.032 ± .003	.037 ± .004	.033 ± .004	.036 ± .004	.035 ± .005			
2	.043 ± .005	.033 ± .004	.033 ± .004	.035 ± .004	.032 ± .004	.042 ± .007	.028 ± .005			
Portal venous								.54	.48	1.00
0	.289 ± .079	.273 ± .065	.286 ± .068	.315 ± .075	.232 ± .010	.250 ± .029	.246 ± .048			
1	.331 ± .035	.307 ± .031	.302 ± .038	.302 ± .026	.286 ± .032	.324 ± .071	.259 ± .071			
2	.325 ± .018	.284 ± .017	.311 ± .012	.328 ± .009	.309 ± .014	.307 ± .030	.224 ± .046			
Hepatic venous								.31	.27	.99
0	.045 ± .014	.035 ± .004	.035 ± .004	.037 ± .006	.030 ± .0002	.032 ± .002	.029 ± .005			
1	.058 ± .006	.051 ± .004	.047 ± .004	.052 ± .007	.047 ± .007	.052 ± .010	.050 ± .008			
2	.066 ± .005	.059 ± .008	.050 ± .005	.051 ± .004	.050 ± .005	.056 ± .007	.044 ± .005			
2-Methyl-propionate										
Arterial								.75	.87	.87
0	.002 ± .0003	.002 ± .001	.003 ± .002	.002 ± .0002	.003 ± .001	.002 ± .001	.002 ± .0001			
1	.004 ± .001	.004 ± .0002	.003 ± .001	.005 ± .001	.003 ± .001	.003 ± .001	.003 ± .001			
2	.004 ± .001	.003 ± .001	.003 ± .0004	.003 ± .0004	.003 ± .0004	.002 ± .000	.003 ± .0005			
Portal venous								.67	.010	.95
0	.016 ± .0002	.016 ± .0005	.014 ± .001	.016 ± .0003	.015 ± .0005	.013 ± .001	.011 ± .0003			
1	.016 ± .0005	.015 ± .001	.016 ± .001	.022 ± .008	.016 ± .002	.012 ± .001	.011 ± .001			
2	.014 ± .002	.015 ± .001	.016 ± .001	.016 ± .001	.016 ± .001	.011 ± .0004	.010 ± .001			
Hepatic venous								.82	.83	.42
0	.004 ± .001	.003 ± .001	.003 ± .001	.003 ± .001	.002 ± .0003	.003 ± .001	.002 ± .0003			
1	.004 ± .0005	.003 ± .001	.004 ± .001	.004 ± .001	.004 ± .001	.003 ± .001	.006 ± .002			
2	.005 ± .001	.004 ± .0005	.004 ± .0002	.003 ± .0004	.004 ± .0003	.003 ± .0004	.003 ± .001			
Butyrate										
Arterial								.28	.008	.78
0	.015 ± .006	.006 ± .001	.010 ± .002	.008 ± .0001	.006 ± .002	.007 ± .002	.005 ± .001			
1	.012 ± .003	.011 ± .001	.010 ± .002	.011 ± .002	.009 ± .003	.009 ± .002	.009 ± .004			
2	.020 ± .002	.016 ± .002	.013 ± .002	.013 ± .002	.012 ± .002	.011 ± .001	.008 ± .001			
Portal venous								.70	.008	.82
0	.086 ± .038	.041 ± .009	.052 ± .005	.052 ± .005	.035 ± .010	.044 ± .001	.037 ± .004			
1	.057 ± .008	.053 ± .007	.053 ± .009	.053 ± .007	.046 ± .008	.049 ± .015	.044 ± .022			
2	.078 ± .008	.066 ± .004	.063 ± .005	.061 ± .006	.054 ± .005	.046 ± .004	.030 ± .007			
Hepatic venous								.12	.0001	.40
0	.033 ± .007	.013 ± .001	.017 ± .000	.015 ± .001	.012 ± .005	.013 ± .002	.010 ± .003			
1	.022 ± .002	.018 ± .003	.018 ± .004	.020 ± .003	.016 ± .005	.014 ± .004	.010 ± .002			
2	.044 ± .006	.031 ± .004	.027 ± .003	.026 ± .003	.024 ± .003	.021 ± .001	.015 ± .003			
2-Methyl- and 3-methyl-butyrate										
Arterial								.36	.50	1.00
0	.007 ± .001	.005 ± .0002	.006 ± .001	.005 ± .001	.005 ± .002	.004 ± .001	.004 ± .001			
1	.006 ± .001	.005 ± .0004	.005 ± .001	.006 ± .001	.005 ± .001	.005 ± .001	.005 ± .001			
2	.006 ± .001	.006 ± .001	.007 ± .001	.006 ± .001	.006 ± .001	.005 ± .001	.006 ± .001			
Portal venous								.45	.0001	.94
0	.021 ± .0002	.021 ± .002	.018 ± .001	.019 ± .0005	.018 ± .001	.015 ± .001	.012 ± .001			
1	.018 ± .001	.018 ± .002	.019 ± .003	.018 ± .001	.018 ± .002	.014 ± .002	.012 ± .001			
2	.024 ± .004	.022 ± .002	.019 ± .002	.021 ± .002	.019 ± .002	.013 ± .001	.012 ± .001			
Hepatic venous								.66	.69	.99
0	.008 ± .001	.006 ± .0003	.006 ± .001	.006 ± .001	.006 ± .001	.005 ± .001	.005 ± .001			
1	.007 ± .000	.006 ± .0004	.007 ± .001	.006 ± .001	.007 ± .002	.006 ± .001	.007 ± .001			
2	.014 ± .006	.009 ± .001	.009 ± .001	.008 ± .001	.008 ± .001	.006 ± .001	.008 ± .001			

(continued)

Table 5 (*continued*). Means and standard errors for concentration (m*M*) of blood volatile fatty acids in pregnant ewes

Item and litter size[a]	Period and days before parturition 1 151 ± 1	2 103 ± 1	3 82 ± 1	4 61 ± 1	5 39 ± 1	6 19 ± 1	7 6 ± 1	Probability Litter	Period	L × P
Valerate										
Arterial								.48	.69	.99
0	.002 ± .001	.003 ± .0002	.002 ± .001	.002 ± .0002	.002 ± .0002	.003 ± .001	.002 ± .001			
1	.003 ± .001	.003 ± .0004	.002 ± .001	.002 ± .001	.003 ± .0003	.002 ± .001	.002 ± .001			
2	.002 ± .001	.002 ± .001	.002 ± .0004	.002 ± .0005	.003 ± .0003	.002 ± .0004	.002 ± .0004			
Portal venous								.67	.04	.77
0	.011 ± .004	.007 ± .001	.008 ± .001	.007 ± .001	.006 ± .0001	.007 ± .0001	.006 ± .001			
1	.009 ± .001	.018 ± .002	.007 ± .001	.007 ± .001	.007 ± .001	.008 ± .002	.007 ± .003			
2	.013 ± .002	.009 ± .005	.009 ± .001	.009 ± .0006	.008 ± .001	.007 ± .001	.005 ± .001			
Hepatic venous								.39	.07	.96
0	.002 ± .0003	.002 ± .0001	.002 ± .0001	.001 ± .001	.002 ± .0001	.002 ± .0004	.000 ± .000			
1	.001 ± .001	.002 ± .001	.001 ± .0004	.002 ± .001	.002 ± .001	.001 ± .001	.001 ± .0007			
2	.002 ± .0004	.002 ± .001	.001 ± .0004	.001 ± .0004	.002 ± .0002	.002 ± .0004	.001 ± .0004			

[a]Litter size 0 Periods 1 through 7 (n = 2). Litter size 1: Periods 1 through 4 (n = 6), Periods 5 through 7 arterial and portal venous (n = 6) and hepatic venous (n = 5). Litter size 2: Periods 1 and 5 (n = 7), Periods 2 through 4 and 7 (n = 8), Period 6 arterial and hepatic venous (n = 8) and portal venous (n = 7).

affect the manner in which nutrients are used by the dam in support of the pregnancy. In order to establish the relationship between fetal nutrient use and maternal metabolism, the patterns of nutrient flux across the PDV and liver of the dam were determined during pregnancy.

Plasma flows followed a pattern similar to that of blood flows: changes in plasma flows followed feed intake patterns during pregnancy (Freetly and Ferrell, 1997)

The glucose turnover rate increases in the pregnant ewe by 37% in late pregnancy (Prior and Christenson, 1978). Net PDV glucose release did not differ from zero. The observation that net PDV release does not differ from zero is consistent with the work of van der Walt et al. (1983); they reported that, in midpregnancy, glucose utilization and production rates are nearly equal in the PDV. In the current study, there was a tendency ($P = .07$) for pregnant ewes to have a higher hepatic glucose release. Hepatic glucose release in ewes with a single fetus increased 26% at 19 d before parturition compared with the same ewes before mating. Estimates of glucose uptake by the gravid uterus in late gestation range from 20 to 48% of the maternal glucose turnover rate (Bergman, 1963; Prior and Christenson, 1978). At approximately 125 d of gestation, the gravid uterus takes up 16.8 mmol/h (Battaglia and Meschia, 1981). This uptake is consistent with the 11.8-mmol/h difference in hepatic glucose production between prebreeding and 19 d before lambing observed in this study. In late pregnancy, 29% of the glucose taken up by the gravid uterus is used by the fetus, and the remaining 71% is used by the uteroplacental tissues. The proportion of glucose used by the uteroplacental tissues in early pregnancy is higher than in late pregnancy in sheep (Bell et al., 1986) and cattle (Reynolds et al., 1986).

Hepatic lactate uptake increases exponentially during pregnancy. With the exception of 19 d before parturition for singles, the change in net splanchnic lactate carbon uptake is equal to or greater than the net change in net hepatic glucose carbon release (Figure 3), which suggests that lactate is an important precursor for gluconeogenesis during pregnancy. Lactate release by the PDV did not change during pregnancy, suggesting that the increase in lactate is not associated with diet. It has been estimated that

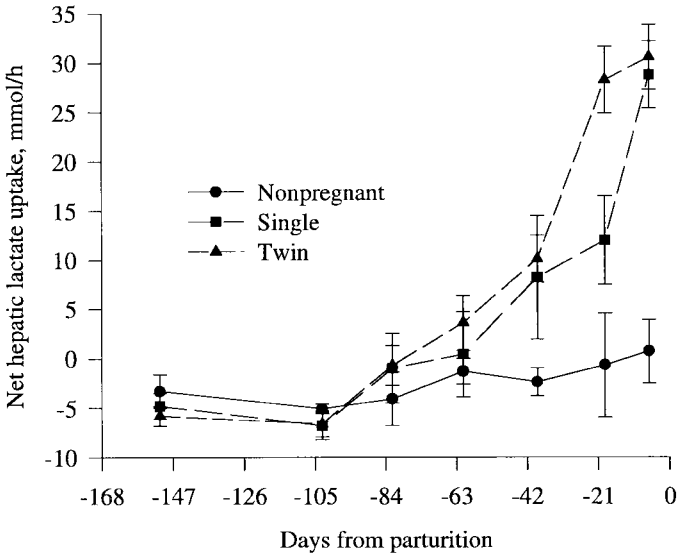

Figure 2. Means and standard errors for net hepatic lactate uptake of ewes. Nonpregnant (n = 2). Single: –151 to –61 d and –19 d (n = 6), and –39 and –6 d (n = 5). Twins: –151, –103, and –82 d (n = 11); –61 d (n = 10); –39 and –19 d (n = 9); and –6 d (n = 8).

Table 6. Means and standard errors for net release (mmol/h) of blood volatile fatty acids across the portal-drained viscera and liver of pregnant ewes

Item and litter size[a]	Period and days before parturition: 1 151 ± 1	2 103 ± 1	3 82 ± 1	4 61 ± 1	5 39 ± 1	6 19 ± 1	7 6 ± 1	Probability: Litter	Period	L × P
Acetate										
Portal-drained viscera								.39	.24	.87
0	175.2 ± 71.6	157.1 ± 6.6	105.9 ± 31.3	133.4 ± 42.3	74.5 ± .5	123.8 ± 2.5	115.7 ± 10.0			
1	170.1 ± 6.7	164.4 ± 17.7	138.0 ± 17.0	156.2 ± 16.1	158.0 ± 19.7	169.7 ± 35.0	141.1 ± 40.1			
2	175.7 ± 8.3	158.4 ± 17.1	164.4 ± 14.1	169.0 ± 10.5	171.0 ± 12.8	192.0 ± 18.7	121.6 ± 22.9			
Hepatic								.24	.64	.95
0	−2.5 ± 6.4	−1.7 ± 9.7	11.7 ± 5.9	−12.6 ± 17.9	19.7 ± 6.7	9.0 ± 8.2	−6.4 ± 2.5			
1	−18.2 ± 16.3	−2.0 ± 7.6	−1.2 ± 6.1	2.7 ± 9.6	5.2 ± 6.1	−4.2 ± 9.0	8.2 ± 7.7			
2	6.2 ± 6.1	8.3 ± 8.1	13.7 ± 4.1	5.1 ± 5.2	9.5 ± 6.6	16.6 ± 12.6	21.2 ± 14.2			
Splanchnic								.26	.24	.90
0	172.7 ± 65.2	155.3 ± 16.3	117.6 ± 25.4	120.8 ± 24.4	94.2 ± 6.3	132.9 ± 10.7	109.3 ± 12.6			
1	151.9 ± 19.1	162.4 ± 11.1	136.8 ± 18.9	158.9 ± 17.8	153.0 ± 20.6	148.6 ± 30.7	115.9 ± 24.6			
2	181.9 ± 8.4	166.8 ± 12.5	178.1 ± 12.1	174.1 ± 6.9	171.0 ± 12.8	197.6 ± 15.1	142.7 ± 29.9			
Propionate										
Portal-drained viscera								.41	.26	.94
0	46.3 ± 19.8	45.9 ± .2	32.7 ± 14.2	40.2 ± 16.1	19.2 ± 2.6	33.5 ± 4.4	31.3 ± 2.6			
1	46.6 ± 3.7	42.7 ± 6.2	38.9 ± 5.9	39.6 ± 5.0	39.1 ± 6.0	50.8 ± 12.3	37.1 ± 12.8			
2	51.2 ± 3.6	39.7 ± 4.3	43.1 ± 2.8	45.4 ± 2.6	44.2 ± 3.4	54.2 ± 6.5	34.2 ± 7.1			
Hepatic								.52	.10	.87
0	−43.2 ± 18.3	−43.2 ± .4	−31.8 ± 12.5	−38.1 ± 15.9	−17.8 ± 2.4	−32.5 ± 2.8	−29.4 ± 2.1			
1	−45.0 ± 4.4	−40.4 ± 5.8	−36.5 ± 5.6	−36.8 ± 4.8	−34.5 ± 6.3	−42.3 ± 12.8	−24.6 ± 10.0			
2	−46.8 ± 4.9	−34.7 ± 5.0	−39.9 ± 2.3	−42.6 ± 2.4	−40.8 ± 3.0	−51.0 ± 6.4	−31.1 ± 6.8			
Splanchnic								.22	.87	.71
0	3.0 ± 1.5	2.7 ± .7	.9 ± 1.7	2.1 ± .2	1.3 ± .1	1.0 ± 1.6	1.9 ± .5			
1	1.6 ± 1.3	2.3 ± .7	2.4 ± .4	2.7 ± .8	2.6 ± .7	3.6 ± 1.1	3.1 ± 1.1			
2	4.4 ± .8	5.1 ± 1.4	3.1 ± .6	2.9 ± .4	3.4 ± .6	3.2 ± .6	3.1 ± .5			
2-Methyl-propionate										
Portal-drained viscera								.34	>.001	.10
0	2.4 ± .4	2.6 ± .7	1.4 ± .4	1.8 ± .4	1.1 ± .1	1.6 ± .2	1.3 ± .2			
1	1.9 ± .1	1.7 ± .1	1.8 ± .2	1.6 ± .3	2.0 ± .3	1.4 ± .3	1.2 ± .2			
2	1.9 ± .2	1.9 ± .1	1.9 ± .1	2.0 ± .2	2.0 ± .1	1.8 ± .2	1.2 ± .1			
Hepatic								.38	.005	.28
0	−2.0 ± .5	−2.3 ± .3	−1.4 ± .2	−1.7 ± .5	−1.2 ± .01	−1.5 ± .2	−1.3 ± .2			
1	−2.0 ± .03	−1.9 ± .1	−1.6 ± .2	−1.7 ± .2	−1.8 ± .4	−1.5 ± .3	−.8 ± .4			
2	−1.6 ± .2	−1.6 ± .2	−1.8 ± .1	−2.0 ± .2	−1.9 ± .2	−1.8 ± .2	−1.2 ± .1			
Splanchnic								.22	.68	.14
0	.4 ± .1	.3 ± .3	.0 ± .2	.1 ± .1	−.1 ± .1	.1 ± .003	.1 ± .03			
1	.0 ± .1	−.1 ± .1	.2 ± .1	−.2 ± .1	−.1 ± .03	−.1 ± .2	.3 ± .2			
2	.3 ± .2	1.3 ± .1	.1 ± .1	.0 ± .1	.1 ± .1	.0 ± .1	.0 ± .1			
Butyrate										
Portal-drained viscera								.76	.03	.82
0	12.9 ± 7.6	6.4 ± .2	5.4 ± 2.3	5.9 ± 1.8	2.5 ± .5	5.5 ± .2	4.5 ± .9			
1	7.7 ± 1.0	7.3 ± 1.4	6.2 ± 1.1	6.2 ± 1.1	5.8 ± 1.3	7.3 ± 2.5	6.5 ± 4.0			
2	10.7 ± 1.7	8.0 ± .9	7.9 ± .9	2.0 ± .2	6.9 ± .8	7.3 ± 1.2	3.9 ± 1.1			
Hepatic								.87	.006	.87
0	−9.6 ± 7.1	−5.0 ± .1	−4.4 ± 1.9	−4.8 ± 1.8	−1.8 ± .2	−4.4 ± .4	−3.6 ± .5			
1	−5.9 ± 1.1	−5.9 ± 1.1	−4.9 ± .9	−4.7 ± 1.0	−4.2 ± 1.1	−4.0 ± 1.5	−1.7 ± .9			
2	−5.8 ± 1.7	−5.3 ± .9	−5.5 ± .7	−5.1 ± .7	−4.7 ± .8	−4.9 ± 1.1	−2.4 ± .7			
Splanchnic								.08	>.001	.44
0	3.3 ± .6	1.4 ± .3	1.0 ± .4	1.1 ± .01	.7 ± .3	1.1 ± .1	.9 ± .4			
1	1.8 ± .3	1.4 ± .4	1.3 ± .3	1.5 ± .4	1.2 ± .5	1.3 ± .4	.9 ± .3			
2	4.9 ± 1.2	2.7 ± .3	2.4 ± .2	2.3 ± .3	2.2 ± .3	2.2 ± .2	1.4 ± .3			
2-Methyl- and 3-methyl-butyrate										
Portal-drained viscera								.51	.002	.70
0	2.4 ± .4	3.0 ± .3	1.5 ± .2	1.9 ± .5	1.2 ± .2	1.6 ± .1	1.2 ± .1			
1	2.0 ± .2	1.9 ± .2	2.0 ± .3	1.8 ± .2	2.0 ± .4	1.6 ± .3	1.1 ± .2			
2	3.1 ± .8	2.5 ± .5	1.9 ± .2	2.3 ± .2	2.0 ± .2	1.6 ± .2	1.1 ± .2			
Hepatic								.50	.25	1.00
0	−2.2 ± .6	−2.8 ± .3	−1.5 ± .2	−1.7 ± .5	−1.1 ± .1	−1.4 ± .1	−1.0 ± .1			
1	−1.8 ± .1	−1.8 ± .2	−1.7 ± .2	−1.8 ± .2	−1.7 ± .5	−1.4 ± .3	−.8 ± .2			
2	−1.6 ± 1.6	−2.1 ± .5	−1.6 ± .2	−1.9 ± .2	−1.7 ± .2	−1.4 ± .2	−.6 ± .1			
Splanchnic								.97	.89	.93
0	.2 ± .2	.2 ± .1	.1 ± .04	.2 ± .001	.1 ± .1	.1 ± .03	.2 ± .002			
1	.2 ± .1	.1 ± .1	.2 ± .1	.0 ± .2	.3 ± .1	.2 ± .1	.3 ± .1			
2	1.5 ± 1.2	.4 ± .1	.3 ± .03	.4 ± .1	.3 ± .1	.2 ± .1	.5 ± .2			

(continued)

Table 6 (*continued*). Means and standard errors for net release (mmol/h) of blood volatile fatty acids across the portal-drained viscera and liver of pregnant ewes

Item and litter size[a]	Period and days before parturition 1 151 ± 1	2 103 ± 1	3 82 ± 1	4 61 ± 1	5 39 ± 1	6 19 ± 1	7 6 ± 1	Probability Litter	Period	L × P
Valerate										
Portal-drained viscera								.48	.02	.61
0	1.5 ± .8	.8 ± .1	.7 ± .4	.7 ± .3	.3 ± .05	.6 ± .1	.4 ± .2			
1	1.0 ± .1	1.2 ± .3	.8 ± .2	.8 ± .1	.7 ± .2	1.1 ± .3	.9 ± .5			
2	1.9 ± .4	1.0 ± .1	1.1 ± .1	1.0 ± .1	.9 ± .1	1.1 ± .2	.6 ± .1			
Hepatic								.64	.001	.69
0	−1.6 ± .9	−1.0 ± .005	−.8 ± .3	−.9 ± .2	−.3 ± .03	−.8 ± .01	−.8 ± .05			
1	−1.2 ± .1	−1.2 ± .3	−.9 ± .2	−.9 ± .1	−.9 ± .2	−.9 ± .3	−.5 ± .2			
2	−1.9 ± .4	−1.0 ± .1	−1.2 ± .1	−1.1 ± .1	−.9 ± .1	−1.1 ± .2	−.7 ± .1			
Splanchnic								.23	.73	.43
0	−.1 ± .1	−.2 ± .1	−.1 ± .1	−.2 ± .1	.0 ± .02	−.1 ± .1	−.4 ± .1			
1	−.2 ± .1	.0 ± .1	.0 ± .1	−.1 ± .1	−.1 ± .1	.0 ± .05	.0 ± .02			
2	.0 ± .1	.0 ± .1	−.1 ± .1	−.1 ± .1	.0 ± .01	.0 ± .03	−.1 ± .1			

[a]Litter size 0 Periods 1 through 7 (n = 2). Litter size 1: Periods 1 through 4 (n = 6), Periods 5 through 7 portal-drained viscera (n = 6) and hepatic and splanchnic (n = 5). Litter size 2: Periods 1 and 5 (n = 7), Periods 2 through 4 and 7 (n = 8), Period 6 splanchnic (n = 8) and portal-drained viscera and hepatic (n = 7).

37% of the glucose taken up by the sheep placenta is released as lactate, with the remainder being oxidized (Meschia et al., 1980). Placental lactate is released both to the fetus and maternal blood. Lactate released into fetal blood is subsequently oxidized, and there is not a net transfer of lactate from the fetal compartment to the maternal compartment (Sparks et al., 1982). Reynolds et al. (1986) demonstrated that, in cattle, lactate release from the gravid uterus increases in an exponential manner. In midpregnancy, 7% of the glucose produced by the liver is from lactate (van der Walt et al., 1983). Net release of lactate in late pregnancy into the maternal blood from the gravid uterus has been estimated to be 3.6 mmol/h (Battaglia and Meschia, 1981). Lactate release by the gravid uterus can account for 24% of the change in lactate carbon taken up by the splanchnic tissues 19 d before parturition. This suggests that other peripheral tissues increase lactate release during pregnancy. Hough et al. (1985) demonstrated that lactate release by the hind limb increases as pregnancy progresses.

In late gestation, the gravid uterus takes up 16.2 mmol/h of α-amino nitrogen (Battaglia and Meschia, 1981). Amino acids that are taken up by the fetus are used for protein accretion and are catabolized for energy. It is estimated that 25% of the fetal energy requirement is met by amino acids (Munro, 1983). During pregnancy, the net splanchnic release of α-amino nitrogen did not differ from zero. It is important to note that not all of the amino acids were catabolized. By subtracting net hepatic urea N production corrected for hepatic ammonia uptake, an estimate of the amino acids available for protein synthesis is obtained (21.6 ± 1.6 mmol/h). This is an underestimate to the extent that catabolism of compounds such as pyrimidines are not accounted for in the urea flux. These amino acids are then available for synthesis of liver and export proteins or are available for release from the liver. If it is assumed that the liver is not accruing protein in late pregnancy, then the amino acids not catabolized by the liver are most likely being exported. The measurement of net α-amino N flux across the splanchnic tissues has a number of limitations that will underestimate the availability of amino acids to peripheral tissues. Amino acids released as export protein or amino acids bound to blood proteins do not quantitatively account for all of the amino acids being released. Also, the use of α-

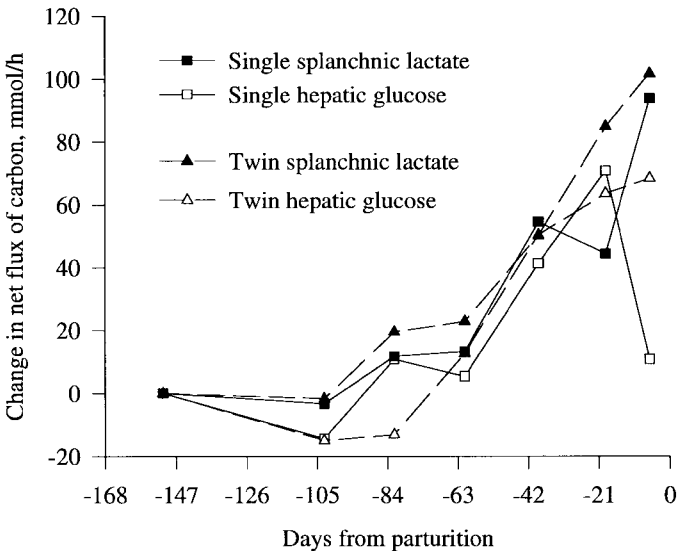

Figure 3. Mean changes in net hepatic glucose carbon release and net splanchnic lactate carbon uptake of pregnant ewes.

amino N flux does not account for the exchange of amino acids at the liver. For example, there may be a net uptake of one amino acid by the splanchnic tissues, yet it may be offset by an equal release of another amino acid. These offsetting fluxes may become quantitatively important with amino acids involved with transamination.

Ammonia and urea are export products of the gravid uterus. In late pregnancy, it is estimated that the uteroplacenta releases 1.8 mmol/h of ammonia into the maternal blood (Battaglia and Meschia, 1981). In the current study, the majority of the hepatic uptake of ammonia can be accounted for by the net release of ammonia from the PDV. There was a net splanchnic ammonia uptake before mating, which suggests that ammonia is being released by peripheral tissue other than the gravid uterus. Estimated ammonia production rates of the gravid uterus are similar in magnitude to the net splanchnic ammonia uptakes observed in this study. In late pregnancy, the gravid uterus releases 7.2 mmol/h of urea nitrogen. Faichney and White (1987) estimated that fetal urea synthesis was 12% of the maternal synthesis rate in late pregnancy. Arterial urea nitrogen concentrations decreased during pregnancy, but this was most likely a function of the decrease in maternal hepatic urea N release. The decreased hepatic urea N release coincides with the decreased PDV ammonia and α-amino N flux.

Even though feed intakes did not differ in this study (Freetly and Ferrell, 1997), it is important to note that feed intakes were numerically their highest (2,501 ± 106 g/d) before mating and were at there lowest (1,699 ± 195 g/d) 6 d before parturition. Period effects for VFA concentration and fluxes were most often the result of high values before mating and lower values 6 d before parturition. Because most of the VFA are a result of microbial fermentation of the feed, we would speculate that differences in their concentrations are due to differences in feed intake. Even though not all VFA concentrations and fluxes differed with periods, the numerical trends support this speculation.

Net splanchnic acetate release exceeds net acetate uptake by the gravid uterus. Char and Creasy (1976) estimated that daily fetal acetate uptake was 23.3 mmol/kg of fetal weight in late pregnancy. If we assume that fetal weight at 19 d before parturition in this study was 2.8 kg, then we would estimate that net fetal acetate uptake was 2.7 mmol/h, which would be less than 2% of the net splanchnic acetate release. Acetate utilization by peripheral tissues changes during pregnancy. Hough et al. (1986b) determined that whole-animal acetate entry rates were higher in pregnant than in nonpregnant-nonlactating ewes and that the oxidation rate of acetate was lower. In the same ewes, Hough et al. (1986a) reported that uptake by the hind limb decreased in late pregnancy and estimated that 7% of the entry rate was taken up by skeletal muscle. The low estimated uptakes by the gravid uterus and skeletal muscle suggest that other tissues are utilizing the acetate being released by the splanchnic tissues. Typically, ewes that are not feed-restricted gain maternal tissue during pregnancy (Rattray et al., 1974), suggesting that acetate may be used by the adipose tissue.

Net splanchnic release of propionate and larger VFA was low compared with acetate. Net hepatic uptake of these VFA was nearly equal to net PDV release. The overall average hepatic extraction ratios for propionate, 2-methyl-propionate, and valerate were similar, with 70 to 80% of the VFA presented to the liver being removed. The extraction ratios for butyrate and 2-methyl- and 3-methyl-butyrate were lower than the above VFA but were still high relative to acetate. Horino et al. (1968) demonstrated that jugular vein infusion in sheep of propionate or butyrate at .025 mmol/kg·min^{-1} and jugular vein injection of valerate or isovalerate at .1 mmol/kg resulted in elevated circulating insulin levels. This elevation in insulin suggests that removal of these VFA from the blood by the liver is important for maintaining metabolic homeostasis. The high extraction ratio for these VFA is not unique to ewes. Casse et al. (1994) found that the extraction ratios for these VFA in lactating cows with or without intramesenteric propionate infusion ranged from .60 for 3-methyl-butyrate to .93 for valerate. These data would suggest that when these VFA are in physiological concentrations, hepatic uptake of these VFA in ruminants follows mass action kinetics.

Horino et al. (1968) determined that acetate did not stimulate insulin release when it was infused at a rate of .025 mmol/kg·min^{-1}. The low insulinogenic potential of acetate would suggest that net acetate release from the splanchnic tissue is an effective carbon shuttle to the peripheral tissues that is independent of insulin and glucose.

In conclusion, the increase in hepatic oxygen consumption during late pregnancy (Freetly and Ferrell, 1997) seems to be partially due to an increase in hepatic glucose production. Changes in hepatic glucose production are consistent with increased glucose utilization by the gravid uterus. The similarity in extraction ratios for VFA over the entire pregnancy suggests that hepatic uptake of VFA follows mass action kinetics and that their uptake by the liver is not regulated during pregnancy. The increase in hepatic lactate extraction ratios in late pregnancy suggests that lactate uptake by the liver is regulated beyond blood concentration differences. The increase in hepatic lactate uptake in late pregnancy suggests that lactate turnover rate increases. The increase in lactate production seems to be a function of production by the gravid uterus and of an increase in lactate production by peripheral tissues.

Implications

In pregnant ruminants, hepatic metabolite flux is strongly associated with metabolite use by the gravid uterus. This study indicates that, as glucose uptake by the gravid uterus increases, gluconeogenesis by the maternal liver increases at a similar rate.

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